

## REMARKS

### STATUS OF THE CLAIMS

Claims 1 – 5 and 7 – 13 were pending in the application. Claim 6 was previously canceled. Claim 1 is amended. Support for the amendment to claim 1 can be found at paragraph [0019] in the specification. Therefore, no new matter is presented.

Reconsideration and re-examination of this application in view of the following remarks is hereby respectfully requested. Applicants note that the previous rejection of claims 4 – 5 for allegedly being indefinite has not been maintained.

### I. REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claims 1 – 5 and 7 - 13 stand rejected as allegedly failing to comply with the written description requirement. The Examiner alleges that there is insufficient description for the terms “geometric isomer”, “stereoisomer”, and “metabolites”. The Examiner claims that applicants have failed to convey possession of these terms as part of the invention at the time of filing.

In reply, applicants point out that claim 1 has been amended to unambiguously define what is meant by the term “metabolite”. Further, the terms “geometric isomer” and “stereoisomer” are well known in the art, and represent small, easily identifiable groups. For example, the term “geometric isomer” represents the cis- and trans- isomeric forms of ospemifene. Applicants respectfully request the Examiner to reconsider and withdraw this rejection.

### II. REJECTION UNDER 35 U.S.C. §103(a)

The Examiner has maintained the rejection of claims 1 – 5 and 7 – 9 and rejects recently added claims 10 – 13 under 35 U.S.C. §103(a) as being obvious over Biskobing (Expert Opinion Invest. Drug; of record) taken with WO 97/32574 (of record) in view of Halonen et al. (US 6,245,819; of record) further in view of Vasu, Council of Medical Research 2000 (of record) and Melander et al. (Eur. J. Clinical Pharmacology, 1978, 14, 441-444; newly applied) as evidenced by famildoc.org (of record).

The Office Action alleged that Biskobing teaches administering ospemifene to treat bone loss but does not teach the treatment of skin atrophy. The Office Action also alleged that WO 97/32574 teaches that the claimed compounds can be taken with other active compounds, and that “food is can be [sic] active agent as it comprises nutrients for the functioning of the body.” The Office Action further alleged that Halonen et al ('819 patent hereafter) disclosed FC127a (=deaminohydroxytoremifene) as well as active metabolites, geometric isomers or stereoisomers thereof (see col. 2 lines 35-59) for the treatment of vaginal dryness and sexual dysfunction (citing the Abstract). Melander et al. teach administering dicoumarol during eating and blood samples were collected at different intervals.

In describing the cited art references, the Examiner relates that:

[B]ioavailability is not taught as claimed however, one of ordinary skill in the art would have been motivated to combine the teaching of [B]iskobing and Melander and compare the rate of absorption of the drug with food as illustrated in the prior art. One skilled in the art would interpret food as active compounds because they contain proteins, fat, carbohydrates etc, therefore would be motivated to administer ospemifene with food. See page 6 of the Office Action.

The Examiner also cites Vasu for the proposition that the bioavailability of certain drugs is enhanced by food, especially drugs that are not readily absorbed orally.

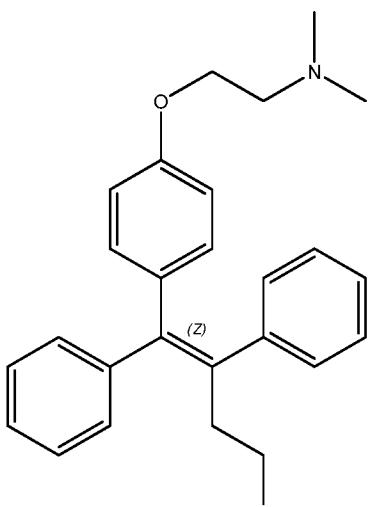
Applicant respectfully maintains that claims 1-5 and 7-13 are not obvious under 35 U.S.C. § 103(a) over Biskobing, WO 97/32574, and the '819 patent, further in view of Vasu and Melander et al. Applicant does not concede there is a *prima facie* case of obviousness. Even assuming for the sake of argument that there is a *prima facie* case of obviousness, Applicant contends that there is sufficient rebuttal evidence to overcome the rejection.

#### *Teaching away*

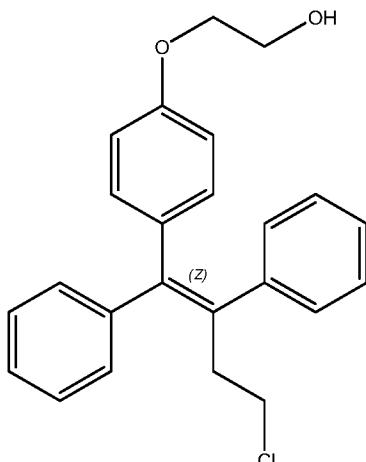
The USPTO must consider rebuttal evidence of teaching away. *See In re Sullivan*, 84 USPQ2d 1034, 1038 (Fed. Cir. 2007) (The Federal Circuit remanded an appeal back to the BPAI for failure to consider rebuttal evidence put forth by the Applicant during prosecution).

Here, Applicant wishes to draw the Examiner's attention to Anttila (1997) European J. Cancer 33 (Suppl. 8), 1144 (“Anttila”) (previously cited in an IDS). Anttila

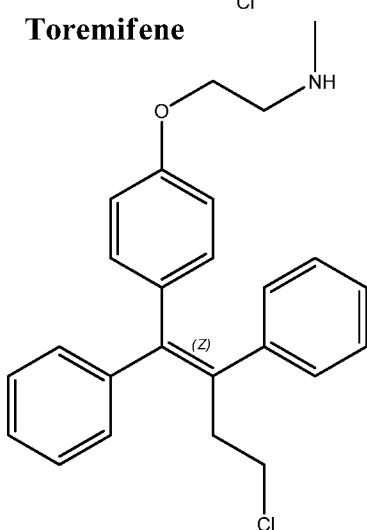
discloses that toremifene “can be taken equally well in fasted conditions or with meals.” The  $t_{max}$  (time to peak concentration) was delayed from 2.3 hours to 4.0 hours, but the  $C_{max}$  (peak concentration), AUC (area under the curve), and  $t_{1/2}$  (half-life) values “were not significantly different” following a 14-hour fast compared to following a standard high-fat meal. In addition, the pharmacokinetic parameters for the active toremifene metabolite N-demethyltoremifene “were similar under fed and fasted conditions.” Thus, Anttila would teach away from the presence of a food effect for triphenylethylenes such as ospemifene. The structures of toremifene, N-demethyltoremifene and ospemifene are reproduced below for the Examiner’s convenience:



**Toremifene**



**Ospemifene**



**N-demethyltoremifene**

In accordance with *In re Sullivan*, Applicant previously requested that the teaching away of the Anttila reference be specifically addressed in the next Office Action. Applicants note that while the Examiner acknowledges this request, she does not specifically address the teachings of Antilla. Instead, she relies on Melander relating a food effect for dicoumarol (a totally unrelated drug) for the proposition that one would “check the bioavailability of food effect on drugs before administration.” Using the Examiner’s analogy that for the claimed invention food can be thought of as a second active ingredient in a combination with ospemifene, the Examiner ignores the closest reference illustrating that food does not work well with toremifene (the parent compound of ospemifene) in favor of a distant reference that food does work well with dicoumarin (a totally unrelated drug). In other words, the Examiner side-steps the question as to what the closest prior art teaches and what would be expected by one of ordinary skill in the art at the time of the invention.

Based on the closest prior art, one of ordinary skill would have expected that administering ospemifene in combination with a foodstuff having nutritional value and causing secretion of bile acids, and taken shortly before, during or after administering ospemifene would have ***no effect*** on bioavailability of ospemifene. That is clearly not the case as shown in the results supporting Applicants’ invention. Applicants respectfully request that the Examiner reconsider the clear evidence teaching away from the claimed invention taught by Antilla.

#### *Unexpected results*

A patent applicant may also attempt to rebut a *prima facie* case of obviousness with evidence of surprising results. *See In re Peterson*, 315 F.3d 1325, 1330-1331 (Fed. Cir. 2003). To date, the USPTO has not acknowledged the unexpected results that are disclosed in the present application. The present application discloses that the effect of food intake on ospemifene absorption is 2-3 fold higher than in the fasted state (page 4, lines 4-5). The effect of food also increases the bioavailability of ospemifene in the fed state as compared to the fasted state. (see e.g., Figures 1 and 2). The Office Action, however, has not shown how one of skill in the art would expect the surprising results

shown in the specification. Applicant respectfully requests that the unexpected results be specifically addressed in the next Office Action or that a Notice of Allowance be issued.

Applicant respectfully maintains that claims 1-5 and 7-13 are not obvious under 35 U.S.C. § 103(a), and respectfully request that this rejection be withdrawn.

### **III. FIRST REJECTION FOR OBVIOUSNESS-TYPE DOUBLE PATENTING**

Claims 1 and 8 – 9 remain rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-12 of U.S. Patent Application No. 11/201,098 (US 2005/0272825). The Office Action alleged that “[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because the claims require the compound ospemifene is administered for the treatment of skin atrophy. As evident by Vasu, drugs are known in the art to be administered, with food. With regard to Applicant's arguing that the disclosure is to enhancing bioavailability will not change treating atrophy, because as soon as the drug is available treating will proceed.”

Applicant respectfully submits that claims 1 and 8 – 9 should not be rejected for obviousness-type double patenting over the '098 patent application. For the reasons set out above in response to the rejection under 35 U.S.C. § 103(a), Applicant similarly maintains that claims 1 and 8 – 9 should not be rejected for obviousness-type double patenting, in view of the teaching away of Anttila, and the unexpected results in disclosed in the specification. Therefore, Applicant respectfully requests that the obviousness-type double patenting rejection of claims 1 and 8 - 9 over US Application No. 11/201,098 be withdrawn.

### **IV. SECOND REJECTION FOR OBVIOUSNESS-TYPE DOUBLE PATENTING**

Claims 1 – 9 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,984,665 (“the '665 patent”). The Office Action alleged that “[a]lthough the conflicting claims are

not identical, they are not patentably distinct from each other. As evident [sic] by Vasu, drugs are known in the art to be administered with food.”

Applicant respectfully submits that claims 1 – 9 should not be rejected for obviousness-type double patenting over the ‘665 patent. For the reasons set out above in response to the rejection under 35 U.S.C. § 103(a), Applicant similarly maintains that claims 1 – 9 should not be rejected for obviousness-type double patenting, in view of the teaching away of Anttila, and the unexpected results in disclosed in the specification. Therefore, Applicant respectfully requests that the obviousness-type double patenting rejection of claims 1 – 9 over the ‘665 patent be withdrawn.

Applicants thank the Examiner for her consideration of this case and submit that the case is in condition for immediate allowance. If the Examiner believes that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at 734-302-6042.

Respectfully submitted,

Dated: September 2, 2008

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